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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/833,203	04/12/2001	Maurice Zauderer	1821.0020001	1700
26111	7590	10/21/2003	EXAMINER	
STERNE, KESSLER, GOLDSTEIN & FOX PLLC			VANDERVEGT, FRANCOIS P	
1100 NEW YORK AVENUE, N.W.			ART UNIT	
WASHINGTON, DC 20005			PAPER NUMBER	

1644

DATE MAILED: 10/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/833,203	ZAUDERER ET AL.	
	Examiner	Art Unit	
	F. Pierre VanderVegt	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 August 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 27-33,35-37,39 and 120-130 is/are pending in the application.
- 4a) Of the above claim(s) 28-30,32,33,35,37,121-123,125-127 and 129 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 27,31,36,39,120,124,128 and 130 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

The Examiner in charge of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to F. Pierre VanderVegt, Ph.D. in Art Unit 1644.

This application claims the benefit of the filing date of provisional application 60/196,472.

Claims 1-26, 34, 38 and 40-119 have been canceled.

Claims 27-33, 35-37, 39 and 120-130 are currently pending.

Election/Restrictions

1. Applicant's election without traverse of Group III, claims 27-39, in Paper No. 7 filed 9-3-02, is again acknowledged. New claims 120-130 are readable on the invention of Group III.

Claims 1-26 and 40-119, readable upon non-elected inventions have been canceled without prejudice.

2. Applicant's election with traverse of the following species: the specific cell surface marker of CEA and the specific antigenic peptide of melanA/MART (51-73), in Paper No. 7 filed 9-3-02 is again acknowledged.

The traversal is on the ground(s) that the cell surface markers are not themselves part of the compound of the present invention, but that the antibodies directed to the markers are part of the recited compounds. This is not found persuasive because the antibodies differ in their antigen binding sites, and said sites are dependent upon the cell surface molecules to which the antibodies are directed to.

The requirement is still deemed proper and is therefore made FINAL.

3. In accordance with the original Restriction requirement and the election of September 3, 2002, **claims 28-30, 32, 33, 35, 37, 121-123, 125-127 and 129 are withdrawn** from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the response filed September 3, 2002.

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4. Accordingly, **claims 27, 31, 36, 39, 120, 124, 128 and 130**, which are readable upon the elected species of CEA as the specific cell surface marker and of melanA/MART (51-73) as the specific antigenic peptide, **are the subject of examination in the present Office Action.**

5. The following represent new grounds of rejection and result in the present Office Action being made **NON-FINAL**. All previous grounds of rejection have been withdrawn.

Response to Arguments

6. Applicant's arguments with respect to claims 27, 31, 36, 39, 120, 124, 128 and 130 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 27, 31, 36, 39, 120, 124, 128 and 130 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 99/64464 (Savage, PM; AL3 on form PTO-1449 filed March 19, 2003) in view of Cormier et al. (Int. J. Cancer 1998 75:517-524; U1 on form PTO-892), Schnell et al. (J. Immunol. 2000 164:1243-1250; V1 on form PTO-892) and Zarour et al. (AR23 on form PTO-1449 filed January 8, 2003).

Savage teaches the making and use of a compound comprising one or more Class I MHC-peptide complexes an antibody or fragment thereof specific for a cell surface marker of a tumor cell (see entire document, Figure 1 in particular), including the elected species of CEA (paragraph bridging pages 5-6 in particular) or for cell surface marker on antigen presenting cells (see entire document, Figure 4 in

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particular. Savage teaches that the MHC molecule is linked to the carboxyl terminus of the antibody (see, for example, Figures 1 and 4 in particular).

Savage differs from the claimed invention in that the publication does not disclose class II MHC molecules or MelanA/MART (51-73) as an antigenic peptide bound to the MHC.

Cormier teaches that MelanA/MART-1 is a melanoma-associated antigen (MAA) that is present in a majority of melanomas (page 571, first column in particular). Cormier further teaches that tumor-infiltrating lymphocytes can recognize MelanA/MART-1 in the context of MHC class I presentation and can be detected in the peripheral blood of patients but "there have been few cases of objective tumor rejection" (page 571, first column in particular). Cormier also teaches that a possible explanation is that down-regulation of MAA by a tumor population provides a mechanism by which tumors escape immune recognition (page 571, second column in particular).

Schnell teaches that it is well established that T cell help can augment CTL function (Abstract in particular). Schnell further teaches that antigen presenting cells that present antigens in the context of both class I and class II stimulate a more robust cytotoxic response to the target tumor (see entire document).

The combination of references differs from the claimed invention in that they do not disclose MelanA/MART (51-73) as an antigenic peptide bound to class II MHC.

Zarour teaches that MelanA/MART (51-73) peptide was able to stimulate *in vitro* expansion of CD4+ T cells and specifically bound to MHC class II HLA-DR4 (see entire document). Zarour further teaches that CD4+ T cell reactivity against the MelanA/MART (51-73) peptide typically coexisted with a high frequency of anti- MelanA/MART (51-73) reactive CD8+ T cells in blood from HLA-A2+/DR4+ patients with melanoma (Abstract in particular).

It would have been *prima facie* obvious to a person having ordinary skill in the art at the time the invention was made to combine the teachings of the references. One would have been motivated with a reasonable expectation of success to create an MHC/antibody compound as taught by Savage to increase the presentation of antigenic peptides on the surface of the tumor cell. The artisan would have been further motivated to use a MelanA/MART antigenic peptide as the target because Cormier teaches that it is present in a majority of melanomas and because there may be down-regulation of MAA in tumor cells to escape immune recognition. The artisan would have been further motivated with a reasonable expectation of success to, based upon the teachings of Savage regarding the class I/antibody constructs, to also make class II/antibody constructs based upon the teachings of Schnell that T cell help (a class II driven event) augments the cytotoxic T cell response (a class I driven event) to tumors and the teachings

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of Zarour that no significant class I CD8+ T cell response were observed in patients in the absence of detectable class II CD4+ T cell response to MelanA/MART-1 (page 403, second column in particular).

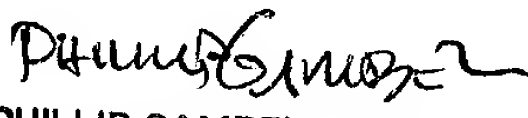
Conclusion

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (703) 305-4441. The examiner can normally be reached on M-Th 6:30-4:00; Alternate Fridays 6:30-3:00. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

F. Pierre VanderVegt, Ph.D. 
Patent Examiner
October 15, 2003


PHILLIP GAMBEL, PH.D.
PRIMARY EXAMINER
TECH CENTER 1600
10/16/03